REMARKS/ARGUMENTS

Claims 1-46 are pending in this application and presented for examination. Claims 1 and 29 (withdrawn) have been amended. No new matter has been introduced. Reconsideration is respectfully requested in view of the remarks below.

I. FORMALITIES

At the outset, Applicant and the undersigned wish to thank Examiner Strzelecka for the telephone interview held on May 13, 2008. During this interview, a number of issues were clarified which have helped Applicant more particularly point out and distinctly claim the inventive subject matter. Applicant thanks Examiner Strzelecka for her time and the courtesy of extending the telephonic interview.

Applicant has amended claims 1 and 29 to more particularly point out and distinctly claim the subject matter of the invention. Support for the amendment is found throughout the specification as filed and more particularly, paragraphs 37-39. As such, Applicant respectfully request that the amendments be entered.

Applicant believes that the foregoing amendment places the application in condition for allowance. As such, withdrawn composition claims 3-17, 20-21, and 25-28 should be rejoined as readable on the allowed claim. In addition, withdrawn process claims 29-46, which are commensurate in scope to the allowed composition claims, should also be rejoined (MPEP § 821.04).

Applicant notes that the polymerase-nucleic complex (PNAC) of the present invention increases the processivity index of the polymerase. Advantageously, the PNAC of the present invention can be a single composition or an array. As disclosed in paragraph 62:

> The PNAC arrays of the present invention can be immobilized on a support in a random fashion (e.g., random X or Y position coordinates), uniform fashion (e.g., regularly spaced X or Y position coordinates) or a combination thereof. As is shown in FIG. 6, in one aspect, the PNAC are isolated into single molecule configuration. This single molecule isolation enables efficient attachment of the PNACs to the support. In addition, it allows for

> efficient single molecule sequencing. Advantageously, the present invention provides single PNACs attached so as to be optically resolvable from their nearest neighbor PNACs. Thus, the PNACs can be analyzed individually without interference from overlapping optical signals from neighboring PNACs. In the present invention, many individual optically resolved PNACs can be sequenced simultaneously.

In view of the amendments above and remarks below, reconsideration is respectfully requested.

II. REJECTION UNDER 35 U.S.C. § 102(b)

The Examiner has maintained the rejection of claims 1-3, 18-19 and 26 under 35 U.S.C. § 102(b) as allegedly being anticipated by Yao *et al.*, *Genes to Cells* (1996) 1 101-113 ("Yao *et al.*"). In response, Applicant respectfully traverses the rejection.

Claim 1 of the present invention recites:

> A polymerase-nucleic acid complex, said polymerase-nucleic acid complex comprising: a target nucleic acid and a nucleic acid polymerase, wherein said polymerase has an attachment complex comprising at least one anchor having a modified amino acid, which irreversibly associates said target nucleic acid with said polymerase to increase the processivity index.

As the Examiner is well aware, in order to anticipate a claim, each and every limitation must be found in the cited reference. In this particular instance, as Applicant has already pointed out, Yao *et al.* in no way teach an anchor having a modified amino acid as is currently claimed. The Examiner states:

> Yao et al. teach modified amino acids on the PCNA and gp45 proteins (page 102, fifth paragraph), therefore anticipating the new limitation.

However, the radioactive label of Yao *et al.* is <u>not</u> part of an attachment complex comprising at least one anchor which irreversibly associates the target nucleic acid with the polymerase, as is currently claimed. In the present invention, the polymerase-nucleic acid

complex comprises an anchor. In order to accommodate the anchor, the polymerase itself must also be modified as an attachment complex.

In Yao *et al.*, the polymerases are wild type polymerases with a sliding clamp and no modification to accommodate an anchor. In fact, the polymerases of Yao *et al.* do not possess an anchor.

Further, Yao *et al.* do not teach an irreversible association between the target nucleic acid with the polymerase. The Examiner states:

> Applicant did not define the term "irreversible association", therefore, any association is considered as irreversible, provided the time scale or topological constraints.

As the Examiner is aware, under MPEP § 2111.01, "the words of a claim must be given their "plain meaning" unless such meaning is inconsistent with the specification." Plain meaning refers to the ordinary and customary meaning given to the term by those of ordinary skill in the art. A skilled person would not interpret "irreversibly associate" as claimed to mean "any association" as the Examiner has contemplated. The Examiner's interpretation eviscerates the plain meaning of the term --irreversibly--. A skilled person would understand this term to mean that association is incapable of being reversed, such as an irreversibly chemical reaction.

The foregoing meaning is inapposite to the teaching of Yao *et al.* Yao *et al.* teach a strategy of "clamp recycling." In this regard, the Examiner's attention is respectfully directed to page 110, left column of Yao *et al.* wherein it states:

> This rapid **cycling off and on the DNA** is a process that would conceptually be hindered by too tight a grip on the DNA such as incurred by a protein ring. The mechanism for this rapid polymerase cycling has been elucidated in *E coli* and T4 phage systems. The DNA polymerase is tightly held to the sliding clamp during chain extension, but upon completing a template the polymerase rapidly dissociates from its clamp. (citations). [Emphasis added].

Further down the same column it states:

> The observed stability of PCNA clamps on DNA suggests that clamp **recycling may be an active process** in eukaryotes as well. [Emphasis added].

The clamps in Yao *et al.* recycle. A skilled person would understand that recycling is NOT an association, which is incapable of being reversed as is currently taught and claimed. As each and every element is not found in the cited reference, the claims are not anticipated. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection.

III. REJECTION UNDER 35 U.S.C. § 102(a)

The Examiner has rejected claims 1-3, 18-19 and 26 under 35 U.S.C. § 102(a) as allegedly being anticipated by Motz *et al*[1]. In response, Applicant respectfully traverses the rejection.

Although Motz *et al.* appears to be silent on the point, there is no reason to believe that the PCNA from *A. fulgidus* is any different from other members of the sliding clamp family of proteins. As such, clamp recycling occurs in Motz *et al.* as in Yao *et al.*

Motz *et al.* state on page 16179, right column:

> Together with the polymerase, the ring appears to move along the DNA as replication proceeds. Such "sliding clamps" exist both for eubacteria (the P-subunit of the polymerase) and for eukaryotes (PCNA), and **the structures of these proteins are almost superimposable** (4). However, the proteins are highly deviant in primary sequence. This situation of sequence divergence and **functional conservation** is also evident for the proteins responsible for loading the sliding clamp onto the DNA. Whereas

[1] It is respectfully noted that the reference to Motz *et al.*, was previously cited in an Information Disclosure Statement filed by Applicant on April 30, 2007 in which the abstract only was submitted. Applicant submits herewith the entire reference with the request that the Examiner include this reference on a PTO-892 for the record.

> in eukaryotes the clamp loader is a heteropentameric complex called RFC (2, 5), the eubacterial clamp loader is represented by the pentameric so called γ-complex (6, 7). [Emphasis added].

Motz *et al.* further state on page 16179, right column:

> Such analyses support the notion that archaebacteria, although possessing metabolic features that are quite similar to bacterial processes, are more **closely related to eukaryotes when translation, transcription, and replication proteins are compared**. For example a clear homologue of PCNA can be found in all published archaebacterial genomes, but no homologues for the eubacterial β-clamp or other eubacterial or other replication factors have been discovered. [Emphasis added].

This evidence of functional conservation suggests that recycling occurs in Motz *et al.* as in Yao *et al.* A skilled person would understand that recycling is NOT an association, which is incapable of being reversed as is currently claimed. As each and every element is not found in the cited reference, the claims are not anticipated. Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection.

IV. FIRST REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claims 19 and 22 under 35 U.S.C. § 103(a) as allegedly being obvious over Motz *et al.* and U.S. Patent No. 5,198,543 ("Blanco *et al.*"). In response, Applicant respectfully traverses the rejection.

As discussed above, claim 1 is patentable. If claim 1 is not obvious then claims 19 and 22 cannot be obvious because they depend from a nonobvious claim. *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992) ("[D]ependent claims are nonobvious if the independent claims from which they depend are nonobvious."). Although Motz *et al.* is silent to the point, there is no reason to believe that the PCNA from *A. fulgidus* is any different from other members of the sliding clamp family of proteins. As such, clamp recycling occurs in Motz *et al.* due to evidence

of functional conservation. A skilled person would understand that recycling is NOT an association, which is incapable of being reversed as is currently claimed.

Blanco *et al.* do not supply the deficiencies of the primary reference. Blanco *et al.* do not teach an attachment complex, nor an anchor having a modified amino acid. Further Blanco *et al.* do not teach a sliding clamp. As such, there is no rational underpinning to support a legal conclusion of obviousness. (*KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (U.S. 2007). Accordingly, Applicant respectfully requests that the Examiner withdraw the rejection.

V. SECOND REJECTION UNDER 35 U.S.C. § 103(a)

The Examiner has rejected claim 23 as allegedly being obvious over U.S. Patent No. 6,255,083 ("Williams") and Motz *et al.* In response, Applicant respectfully traverses the rejection.

Again, claim 1 is patentable. If claim 1 is not obvious then claim 23 cannot be obvious because it depends from a nonobvious claim. *In re Fritch*, 972 F.2d 1260, 1266 (Fed. Cir. 1992) ("[D]ependent claims are nonobvious if the independent claims from which they depend are nonobvious.").

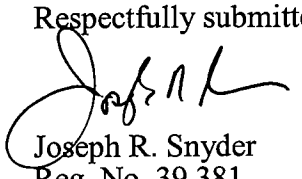
In the method of Williams, amplification of the nucleic acid is unnecessary (*see*, col. 1, lines 58-60). However, Motz *et al.* teach that the principles should be used to develop PCR enzymes (*see*, last line of Motz *et al.*). Because the purpose of the process in Motz *et al.* is unnecessary for the methods of Williams, there is no rational underpinning to support a legal conclusion of obviousness. (*KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1396 (U.S. 2007).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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